Sleep Aspects and Sleep Disorders in Children and Adolescents

Sameh Morkous MD, FAAN

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Sameh Morkous, MD, FAAP, FAAN

Chief, Pediatric Neurology Division

Pediatric Sleep Medicine Medical Director, Lehigh Valley Health Network (LVHN)

Associate Professor, Morsani College of Medicine University of South Florida (USF)

Clinical Professor, Philadelphia College of Osteopathic Medicine (PCOM), and DeSales University, Allentown, PA

PRESENTATION OUTLINE

- Review of normal sleep physiology
- Neurocognitive effects of sleep disruption
- Common sleep disorders
  - Insomnia
  - Sleep Disordered Breathing
  - Non-REM Parasomnias

SLEEP STUDY METHODS

- Ambulatory Techniques
  - Actigraphy (Commonly used, developed in the early 1970s and has come into increasing use in both research studies and clinical practice; allows for the study of sleep-wake patterns and circadian rhythms via the assessment of body movements. The device is typically worn on the wrist and can easily be adapted for home use)
- Survey Instruments
  - Many exist for detecting problematic sleep in children and adolescents, including self-report questionnaires (such as the Child and Family Sleep History Questionnaire and the Pediatric Sleep Questionnaire (PSQ), sleep diaries, and parent report forms)

Fig. 1 Example actigraphy report. Example actigraphy report (participant 5). Sleep patterns are displayed for individual days. The vertical black bars and

EEG SLEEP PATTERNS

Awake	Low Voltage, Random, Fast 
Drowsy	8-12 Hz, Alpha Waves 
Stage 1	3-7 Hz, Theta Waves 
Stage 2	12-14 Hz, Sleep Spindles and K-Complexes 
Stage 3/4	0.5-2 Hz, Delta Waves, High Voltage, Slow Waves 
REM	Low Voltage, Random, Fast with Sawtooth Waves 

NON-REM PHYSIOLOGICAL CHANGES

- Reduced physiological activity
- Autonomic slowing
- Maintain thermoregulation
- Episodic, involuntary movements
- Few rapid-eye movements
- Few penile erections/limited vaginal lubrication
- Reduced blood flow

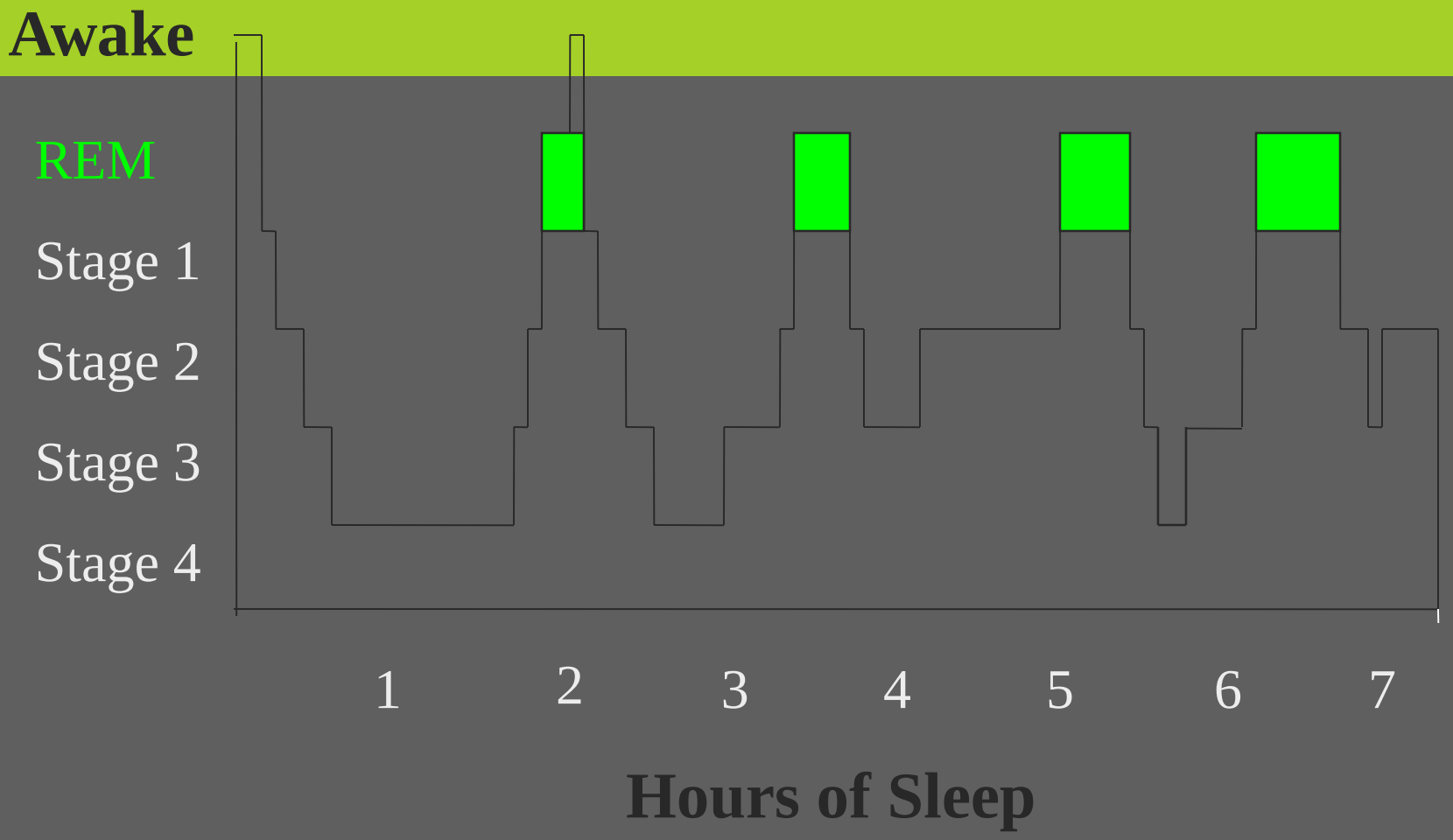
REM PHYSIOLOGICAL CHANGES

- Increased physiological activity
- Autonomic activation
- Altered thermoregulation
- Partial or full penile erections/significant vaginal lubrication
- Skeletal muscle paralysis
- Rapid-eye movements

THE SLEEP CYCLE

- Cyclic nature of sleep is reliable
- Rapid eye movement (REM) periods every 60 minutes (children) & 90 minutes (adults)
- Most REM occurs earlier in sleep in younger children and later in adults
- Stage 3 and REM decrease with age
- Emergence of REM and non-rapid eye movement (NREM) sleep occur over the first 3-6 months of age
- The 3 stages of NREM sleep (N1,N2,N3) can be differentiated at 6 months of age

NORMAL SLEEP CYCLE IN CHILDREN



NEUROENDOCRINE ACTIVITY IN SLEEP

- Sleep promotes:

-Growth hormone (GH)

-Luteinizing hormone (LH)

-Prolactin (PRL)

- Sleep inhibits:

-Adrenocorticotropic hormone (ACTH)

-Thyroid Stimulating Hormone (TSH)

FUNCTIONS OF SLEEP

- Restorative/homeostatic
- Thermoregulation/energy conservation
- Consolidation of learning and memory
- Immune system: The immune system also relies on sufficient quantity and quality of sleep and deficiency in sleep is linked to difficulty fighting infection and increased risk of sickness
- Growth and development: Stage N3 triggers the release of growth-promoting hormones, which boost muscle mass and repair cells and tissues in the body

SLEEP RECOMMENDATIONS FOR PEDIATRIC POPULATIONS: *A consensus statement of the American Academy of Sleep Medicine*

➢ **Consensus recommendations***

- Infants **4 months to 12**: 12-16 hours per 24 hours (including naps)
- Children **1 to 2 years**: 11-14 hours per 24 hours (including naps)
- Children **3 to 5 years**: 10-13 hours per 24 hours (including naps)
- Children **6 to 12 years**: 9-12 hours per 24 hours
- Teenagers **13 to 18 years**: 8-10 hours per 24 hours

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NEUROCOGNITIVE EFFECTS OF SLEEP DISRUPTION:

- Studies show that short sleep in adolescents is associated with the following*:
  - Poor school performance
  - Obesity
  - Metabolic dysfunction and cardiovascular morbidity
  - Increased depressive symptoms
  - Suicidal ideation
  - Risk-taking behaviors
  - Athletic injuries
- Insufficient sleep also is associated with an increased risk of motor vehicle accidents, which account for 35 percent of all deaths and 73 percent of deaths from unintentional injury in US teenagers. Research suggests that crash rates decline by 16.5 percent following a school start time delay of 60 minutes *
- California Dreams Fulfilled for Teens: Governor Newsom signs SB328, the school start time bill; October 13,2019 https://www.startschoollater.net/press-releases/california-dreams-fulfilled-for-teens-governor-newsom-signs-sb328-the-school-start-time-bill

**American Academy of Sleep Medicine April 14th, 2017*

SLEEP DISORDERS IN CHILDREN

- Approximately 25% of children will suffer some type of sleep problem at some point during childhood.
- Complaints range from bedtime resistance and anxiety to primary sleep disorders, such as OSA and narcolepsy.
- Research is consistent with parents reporting 50% of preschool children, 30% of school aged children, and 40% of adolescents as having sleep difficulties,
- Self-report among adolescents reveals 14 – 33% complaining of frequent or extended nighttime awakenings, Excessive Daytime Sleepiness (EDS) , unrefreshing sleep, early insomnia, and a subjective need for more sleep.

INTERNATIONAL CLASSIFICATION OF SLEEP DISORDERS -THIRD EDITION (ICSD-3)

ICSD -3 has 7 major diagnostic detections

- Insomnia
- Sleep-related breathing disorders
- Central disorders of hypersomnolence
- Circadian rhythm sleep-wake disorders
- Parasomnias
- Sleep-related movement disorders
- Other sleep disorders

NARCOLEPSY

- Irresistible bouts of sleep
- Cataplexy *(can be subtle in children, orofacial , with no clear association with emotions in comparison to adults)*
- Sleep paralysis
- Hypnagogic or hypnopompic hallucinations and vivid dreams
- Abnormal sleep-onset REM periods and disturbed nocturnal sleep (sleep fragmentation)

Not all features of this pentad must be present initially.

TREATMENT

- Behavioral
- Pharmacologic
  - Cataplexy and REM related symptoms
    - Selective serotonin reuptake inhibitors (SSRIs)
    - Norepinephrine reuptake inhibitors (NRIs)
    - Tricyclic antidepressants (TCAs)
    - Monoamine oxidase inhibitors (MAOIs)
    - Gamma-hydroxybutyrate (GHB)
  - Excessive daytime sleepiness
    - Armodafinil and Modafinil *(Modafinil is preferred in children:* FDA-approved for children older than 17 years*)*
    - Amphetamines *(Methylphenidate is the second best in children)*
    - Gamma-hydroxybutyrate (GHB)

NARCOLEPSY

- Gamma-hydroxybutyrate GHB (Xyrem) is the only FDA-approved medicine indicated for the treatment of both cataplexy or Excessive Daytime Sleepiness (EDS) in patients 7 years of age and older with narcolepsy

- Jazz Pharmaceuticals announced FDA Approval of Xyrem® (sodium oxybate) for the treatment of cataplexy or EDS in pediatric narcolepsy patients in *Oct 29, 2018*

INSOMNIA

The International Classification of Sleep Disorders – Third Edition (ICSD-**3**) includes:

- A report of sleep initiation or maintenance problems—despite adequate opportunity and circumstances to sleep and with daytime consequences

- The ICSD-3 duration criterion for chronic insomnia disorder is 3 months, and a frequency criterion (at least 3 times per week) has been added

PEDIATRIC INSOMNIA

- Prevalence estimated at 1 – 6 % in general pediatric population but considerably higher amongst those children with neurodevelopment delay and chronic medical conditions

- A study of 46 children (5-16 y/o) found that 50% of the those presenting to a pediatric sleep center for insomnia had another psychiatric diagnosis. In the remaining 50%, although parents denied any previous psychiatric history, 40% displayed psychiatric symptoms—documented by psychometric measures and clinical interviews—which suggests that comprehensive psychometric assessments are warranted in this population (Ivanenko et al. 2004; updated Alfano et al. 2009; Moturi et al. 2010)

BEHAVIORAL INSOMNIA

- The child is unable to fall asleep and/or has prolonged nocturnal awakenings

***There are 3* subtypes:**

1. The limit-setting type is demarcated by behaviors of stalling or refusing going to bed that are attributable to an inadequate limit setting by the parent or caregiver
2. The sleep-onset association type reflects the child's dependency on a specific activity/behavior/ stimulation, typically objects or settings, for initiating sleep or returning to sleep following an awakening. When these are absent, sleep onset is significantly delayed
3. The mixed hybrid type is characterized by features of both sleep-onset association difficulties and bedtime resistance

TREATMENT OF INSOMNIA (1) : SLEEP HYGIENE

- Identify the cause or other Axis I disorder (if possible) and treat
- Healthy sleep habits *at night*
- Dedicate at least 30 minutes of wind-down time before bedtime in which you do something relaxing, such as read a book
- Dim the lights in the house slightly for an hour or so before bed
- Disconnect electronics: Stay away from light-emitting devices such as television, laptops, phones, and tablets—the blue light from their screens can alert the brain
- Use the bed and bedroom for sleep and sex only
- Establish a regular pre-bedtime routine and a regular sleep/wake schedule
- Avoid alcohol or heavy meals too close to bedtime
- Create a sleep-promoting environment that is dark, cool, and comfortable
- Avoid disturbing noises: consider a bedside fan or white-noise machine to block out disturbing sounds

SLEEP HYGIENE (CONTINUED)

- Observe healthy sleep habits *during the day*
- Avoid caffeine, particularly after noon
- Exercise regularly, earlier during the day, but not within the 3 hours before bedtime
- Avoid naps, particularly longer than 20 minutes and outside the 1:00-3:00 PM time window. Keep a sleep diary to identify sleep habits and patterns that you can share with your doctor

COGNITIVE-BEHAVIORAL THERAPY TECHNIQUES SESSIONS (STANDARD)*

- *Sleep restriction*: Restrict actual time spent in bed to enhance and increase the homeostatic drive for sleep, enhance sleep depth and consolidation, improve sleep onset and maintenance
- *Stimulus control therapy*: Associate behaviors conducive to sleep with the activity of falling asleep, imprint bed and bedroom as sleep stimulus
- *Cognitive therapy:* Address dysfunctional beliefs and attitudes about sleep
- *Relaxation training*: Decrease psychological and cognitive hyperarousal and anxiety
- *Circadian rhythm entrainment:* Reinforce or reset biological rhythm using light and/or chronotherapy
- *Cognitive-behavior therapy* : Combination of behavioral and cognitive approaches listed above

*J Clin Sleep Med 2008;4(5):487-504

COGNITIVE-BEHAVIORAL THERAPY TECHNIQUES SESSIONS (STANDARD)*

- ***Sleep restriction***: Restrict actual time spent in bed to enhance and increase the homeostatic drive for sleep, enhance sleep depth and consolidation, improve sleep onset and maintenance

-Go to bed and wake up at the same time every day. Even if you have difficulties falling asleep and trouble awakening in the morning because you are tired, try to get up at the same time (weekends included). This can help adjust your body's clock and aid in falling asleep at night. Go to bed at the time you fall asleep and gradually reduce your sleep time to achieve your bedtime goals

- ***Stimulus control therapy***: Associate behaviors conducive to sleep with the activity of falling asleep, imprint bed and bedroom as sleep stimulus

- If unable to fall asleep within 20 minutes, get up and return to another space in the house to engage in a relaxing activity, such as reading or listening to music. You want bed to conjure sleepy thoughts and positive feelings only

TREATMENT OF INSOMNIA (2): MEDICATION

- No FDA approved treatments
- Sedatives are short-term solutions
- A shorter half-life is typically preferred
  - Alpha-2 agonists (***clonidine***, guanfacine)
  - Sedating antihistamines (diphenhydramine, hydroxyzine, ***cyproheptadine***)
  - Benzodiazepines and similar agents(Sonata, Ambien, Lunesta)
  - Sedating antidepressants (trazodone, Remeron, low dose 1-3 mg doxepin and TCAs)
  - *Gabapentin*
  - *Ramelteon (Rozerem)*
  - Other agents: ***Melatonin*** *improves sleep latency and sleep time by about 30 minutes, prolonged release melatonin available with half life of 7 hours versus 30-50 minutes in immediate release, 1-10 mg 30 minutes before bed to induce sleep and 0.3-0.5 mg 4-5 hours before desired sleep time for circadian phase effect*. Kava, valerian , L-tryptophan, chamomile, passion flower and lavender.

INSOMNIA CASE

- Sam is a 12-year-old male with a childhood history of anxiety. He has a history of mild to moderate sleep disruption (primarily early and occasional middle insomnia) but over the past 6 weeks he has suffered increasing insomnia concurrent with an increase in school stressors. He presents to us with complaints of going to bed at 11 p.m. on weekday and 12 a.m. on the weekends . He will lie in bed for 1-1.5 hours to fall asleep 4-5 x/ week and will wake up at 6 a.m. weekdays and 11 a.m. weekends. He will have nightly nocturnal awakenings 2-3 x/ week with difficulty falling back to sleep for up to 45 minutes.

- *How do we proceed ?*

OBSTRUCTIVE SLEEP APNEA SYNDROME (OSA)

- Prevalence is 1 %-4%
- In prepubertal children, prevalence is equal in boys and girls. In adolescence, prevalence is higher in males
- Habitual snoring occurs in 7-9 % of children at age 4-5 years and 5% at age 10 years
- More likely to present with ADHD symptoms in children

SLEEP DISORDER BREATHING CLINICAL PRESENTATION

Parents complain of:

- Snoring
- Frequent awakenings
- Excessive daytime sedation *(typically more in adults than children*)
- Poor academic performance
- Irritability
- Poor executive function
- Inattention/general cognitive impairment

INTERNATIONAL CLASSIFICATION OF SLEEP DISORDERS – THIRD EDITION (ICSD -3)

The criteria for pediatric OSA have been simplified in the ICSD-3:

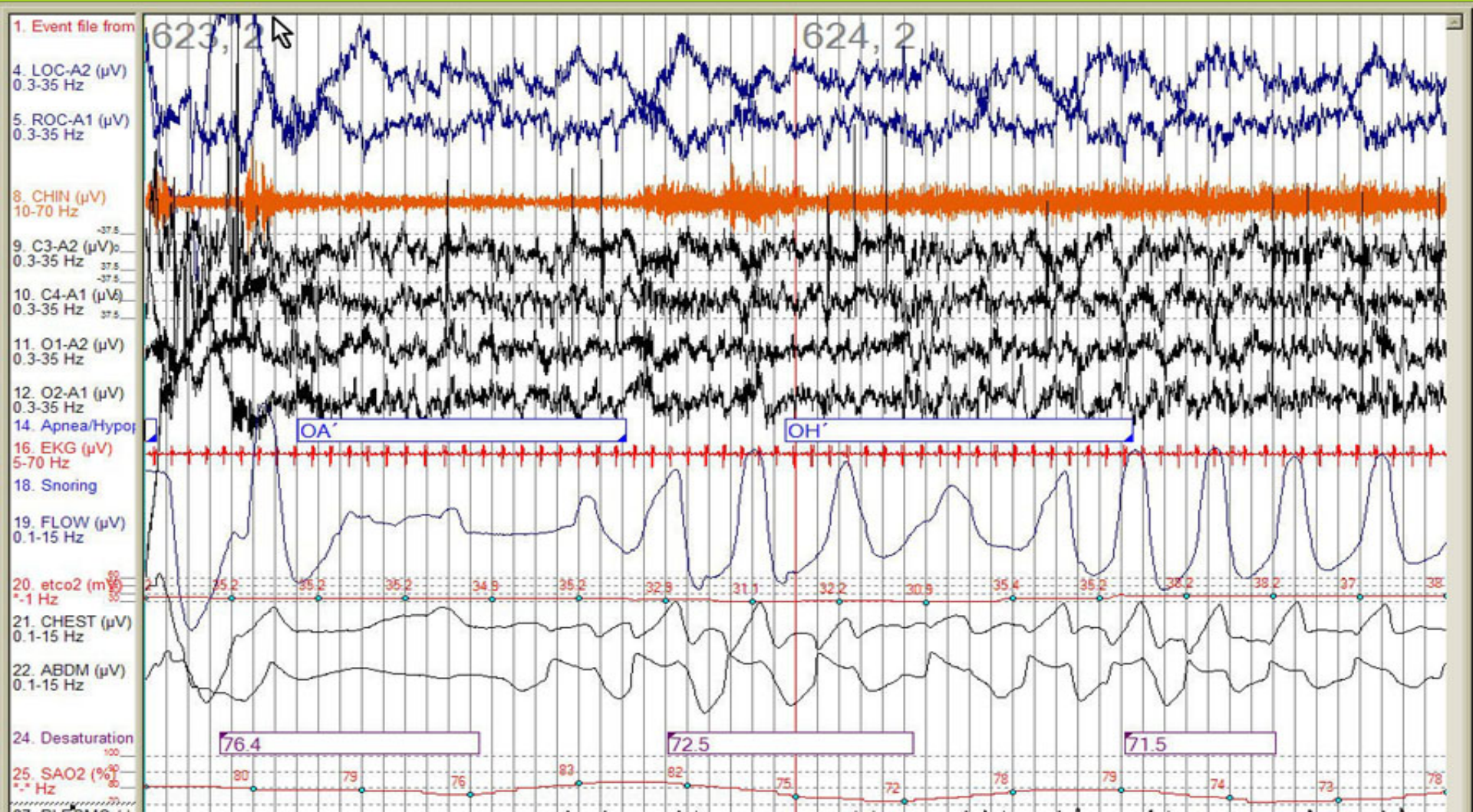
- Signs and symptoms are consolidated into a single criterion. One of these findings (snoring, labored/obstructed breathing or daytime consequences (sleepiness, hyperactivity, etc.) must be present

- The polysomnography (PSG) criterion for diagnosis requires:

1. Either one or more obstructive events (obstructive or mixed apnea or obstructive hypopnea) per hour of sleep (Apnea–Hypopnea Index (AHI) is an index used to indicate the severity of sleep apnea) or;

2. Obstructive hypoventilation, manifested by partial pressure of carbon dioxide ($PaCO_2$) 50 mm Hg for 25% of sleep time, coupled with snoring, paradoxical thoracoabdominal movement or flattening of the nasal airway pressure waveform

OBSTRUCTIVE SLEEP APNEA (OSA)



PEDIATRIC OBSTRUCTIVE SLEEP APNEA SYNDROME (OSA) SEVERITY

- AHI **1.5-4** and 86-91% oxygen desaturation: **mild** OSA
- AHI **5-10** and 76-85% oxygen desaturation: **mild to moderate** OSA
- AHI **>10** and less than 75% oxygen desaturation: **moderate to severe** OSA

OPTIONS INFORMED BY SLEEP STUDY RESULTS

- If AHI < 5
  Watchful waiting or treat with anti-inflammatory agents like montelukast and intranasal steroids for 6 weeks

- If AHI > 5
  Tonsillectomy and Adenoidectomy (T&A)

DIVING DEEPER: *Rethinking AHI as the primary measure of OSA severity* *

- In the study by Kainulainen *et al.* published by *Journal of Clinical Sleep Medicine* Agust,2019, the investigators assessed the correlation between excessive daytime sleepiness (EDS) and novel polysomnographic parameters, including obstruction duration, desaturation duration, desaturation severity, and obstructive severity

- Compared with the Apnea-Hypopnea Index (AHI) or oxygen desaturation index (ODI), the authors found a stronger correlation between EDS and these newer measures

- Although novel, these measures could be scalable

*Cielo CM, Tapia IE. Diving deeper: rethinking AHI as the primary measure of OSA severity. J Clin Sleep Med. 2019;15(8):1075–1076

TREATMENT OF OBSTRUCTIVE SLEEP APNEA

- Weight loss
- Tonsillectomy and Adenoidectomy (T & A)
- Success rate varies (59.8 %) based on curative AHI of less than 1
- High failure rate in obese patients, older than 7 years and with comorbid asthma/complex patients with dysmorphic features and genetic syndrome
- CPAP (Continuous Positive Airway Pressure) prevents obstruction by soft-tissue and keeps airway open if significant residual sleep apnea
- Other surgical intervention (e.g. deviated septum, lingual tonsil)
- Avoid sedatives (which can prevent reawakening to breathe)

INTERNATIONAL CLASSIFICATION OF SLEEP DISORDERS-THIRD EDITION (ICSD-3) PARASOMNIA

- NREM-related parasomnia

-Confusional arousals

-Sleepwalking

-Sleep terrors

-Sleep-related eating disorder

- REM-related parasomnias

-REM sleep behavior disorder

-Recurrent isolated sleep paralysis

-Nightmare disorder

▶Other parasomnias

-Exploding head syndrome

-Sleep-related hallucinations

-Sleep enuresis

-Parasomnia due to a medical disorder

-Parasomnia due to a medication or substance

- Parasomnia, unspecified

NON-REM SLEEP PARASOMNIAS: SHARED FEATURES

- General criteria from the International Classification of Sleep Disorders for arousal disorders include:

(a) recurrent episodes of incomplete awakening

(b) absent or inappropriate responsiveness

(c) limited or no cognition/ dream report

(d) partial or complete amnesia for the episode

(e) episodes typically occur several times per month

- Typically in the first part of the night during slow wave sleep
- Last 1 – 30 minutes
- Retrograde amnesia
- Family/personal history
- More common in childhood
- Attempts to awaken are fruitless
- Psychopathology rare in children

NON-REM SLEEP PARASOMNIAS: PRECIPITATING FACTORS

- Sleep deprivation
- Medications (Zolpidem /Ambien and other benzodiazepine receptor agonists (BZRAs), Tricyclic antidepressants (TCAs) and Lithium)
- Underlying sleep disorders like obstructive sleep apnea or restless legs syndrome
- Anxiety or stress
- Depression or other mental illness
- Nicotine, alcohol, and illicit drugs in older patients
- Gastroesophageal reflux
- Fever

CONFUSIONAL AROUSAL

- Epidemiology
  - No gender differences noted
  - 17.3 % in children 3-13 years old
- Hallmarks include irrational acts, poor judgment, incoherence, and disorientation
- Complete amnesia
- Typically benign, although the occasional patient can become aggressive and violent
- Most episodes are expected to diminish in frequency after 5 years of age

SLEEPWALKING

- Common occurrence
  - Prevalence 6-17% in children; lifetime prevalence is 18.3-40 %
  - Prevalence 4.3 % in adults
- Can be coupled with enuresis
- No consistent gender differences
- Complete amnesia
- Sleepwalking meets the general criteria for NREM arousal disorders and is associated with ambulation
- May engage in complex behaviors
- Strong genetic component (80% with family history of sleep walking or a parasomnia)

SLEEP TERRORS

- Infrequent occurrence
  - Prevalence 1–6.5% in children, 1–2.6% in adults
- Autonomic activation (diaphoresis)
- 30 seconds – 3 minutes
- Subsequent lack of recall
- Gender preference
  - Males more typically in childhood
  - Females possibly more common in adulthood

SLEEP TERRORS VS NIGHTMARES*

TABLE 1
Comparison of Night Terrors and Nightmares

Factor	*Sleep Terrors*	*Nightmares*
Age	3 to 8 years	Any age
Gender	Male predominance	Either
Occurrence in sleep cycle	NREM	REM
Arousable?	No	Yes
Memory for event	None	Yes
Exacerbated by stress	Yes	Yes

REM = rapid eye movement; NREM = non-rapid eye movement.

*https://io9.gizmodo.com/night-terrors-the-real-reasons-why-you-wake-up-screami-1536052042

DIFFERENTIATING EPILEPSY AND AROUSAL DISORDERS

	Epilepsy	Arousal Disorders
Age at onset	Any age	Usually childhood
Frequency	Nightly	Several/month
Event onset	Abrupt	Gradual
Semiology	Stereotyped; hypermotor features	Variable; no hypermotor features
Distribution	Repetitive, clusters	First 1/3 of night; isolated
Event duration	< 1 minute (shorter)	Several minutes (longer)
Sleep stage	N2 > N3	N3
Natural history	70% respond to AEDs	Spontaneous remission

TREATMENT OF NON-REM PARASOMNIAS: PSYCHOSOCIAL INTERVENTIONS

- Family/patient education
- Avoid possible precipitants
- Treating an underlying sleep disorder (sleep apnea or restless legs syndrome)
- Behavioral modifications
- Avoid sleep disruptions
  - Loud noises, limit evening oral fluid intake
- Safeguard the home
  - Movement sensors, locks on windows, remove potentially lethal objects, etc.

TREATMENT OF NON-REM PARASOMNIAS: MEDICATION

- There are no evidence-based treatment guidelines at present; however, low-dose medications have been used, especially if there are concerns about injury to self or others or if the parasomnia persists

- Benzodiazepines
  - Clonazepam, diazepam

- Tricyclic antidepressants

- Selective serotonin reuptake inhibitors (SSRIs) and trazodone

CONCLUSION

- ICSD-3 diagnostic criteria have been revised for many disorders. It is essential for sleep medicine physicians and other providers to familiarize themselves with these change (*https://medicinainternaelsalvador.com/wp-content/uploads/2017/03/internation-classification-ICSD-III-beta.pdf*)
- Use behavioral therapy to treat insomnia in combination with possible medications
- Tonsillectomy and Adenoidectomy (T&A) results in reduction of AHI in children but a large percentage are not "cured". Age, BMI, and co-morbid medical conditions are the best predictors of children that will not completely respond to T&A for OSA
- Know the differences between "Arousal Disorders" and "Epilepsy": misdiagnosis is frequent

USEFUL LINKS

1. Sleep Hygiene handout for patients and families

http://www.cci.health.wa.gov.au/docs/Info-sleep%20hygiene.pdf

2. Pediatric Sleep questionnaire (PSQ) - American Thoracic Society

https://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/psq.php and
http://www.mcbg.org/internal/services/sleep_center/documents/sleeppeds.pdf

3. CONTINUUM: Lifelong Learning in Neurology - LWW Journals

https://journals.lww.com/continuum/pages/default.aspx

4. Journal of Clinical Sleep Medicine (JCSM)

http://jcsm.aasm.org

5. International Classification of Sleep Disorders-Third Edition Highlights and Modifications

https://medicinainternaelsalvador.com/wp-content/uploads/2017/03/internation-classification-ICSD-III-beta.pdf

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Thank you